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EXAMINER	
YANG, NELSON C	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,642	COHEN, JONATHAN M.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Specification

1. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

2. Claim 8 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In claim 1, applicant specifies "a target molecule". In claim 8, applicant broadens this limitation to "a plurality of target molecules" provided from "a plurality of sources"

3. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Applicant has not disclosed the limitation of mounting a plurality of different oligonucleotides to a solid support in the specification.

∧ recited in claim 11

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a step that correlates the extent of stain binding to the target molecule with the clinical utility of the target molecule. Without such a correlation step the body of each claim is just a method for determining whether a stain has bound to a target molecule, which is not consistent with the preamble of each claim.

6. The term "large" in claim 1 is a relative term which renders the claim indefinite. The term "large" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear the quantity of tissue samples the applicant is referring to, as well as the measurement that is being used. Large could be used to refer to number of samples as well as to the volume of samples. This is also applicable to the use of the term "large" in claim 9.

7. Claim 2 provides for the use of a tissue microarray, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

8. Claim 3 provides for the use of an automated stainer, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is

intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

9. Claim 4 provides for the use of both a tissue microarray and an automated stainer, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Claim 6 recites the limitation "said target" in the last line of the claim. There is insufficient antecedent basis for this limitation in the claim.

10. Claim 10 recites the limitation "said tissue sample" in line 4. There is insufficient antecedent basis for this limitation in the claim.

11. Claim 11 recites the limitation "a plurality of different oligonucleotides mounted to a solid support". It is unclear why this limitation was included, as the applicant does not refer to oligonucleotides in the independent claim or in the specification. This limitation is currently interpreted to be in reference to page 16, lines 21-27 regarding detection of DNA, RNA or protein targets in each of the hundreds of specimens in the array.

12. Claim 15 recites the limitation "the apparatus" in the preamble. There is insufficient antecedent basis for this limitation in the claim. Furthermore, claim 15, a product claim, depends from a method claim (claim 14), which is improper. This also applies to the limitation "the apparatus" set forth in claim 16.

13. Claim 17 recites the limitation "said machine" in line 5. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 101

14. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

15. Claims 2-4 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 1-13, and 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leighton [US 6,103,518], in view of Kalra et al [US 6,495,105].

With respect to claims 1, 9, and 10 Leighton teaches a method for evaluating the clinical utility of target molecules comprising the steps of providing a large quantity of different tissue samples, providing a target molecule, providing a stain that specifically binds to said target molecule *in situ*, applying in a high-throughput manner said stain to said tissue samples and

determining the extent to which said stain has bound to said target molecule in said tissue samples. Specifically, Leighton discloses the use of a tissue chip, "a thin section of a tissue microarray that permits massive parallel processing of biological samples, making it possible for researchers to simultaneously compare a variety of molecular markers--DNA, RNA, and protein--in cancer tissues from hundreds or thousands of patients," allowing for the simultaneous testing of thousands of patient tissue. (column 1, lines 30-43). Furthermore, Leighton teaches the staining of tissue samples to reveal structures of interest [column 7, lines 52-57]. Leighton does not teach the use of an automated stainer or applying the stain to the tissue samples in a high throughput manner. However, Kalra et al teaches that modern laboratories find it desirable to automate the staining process in order to examine large numbers of tissue specimens (column 1, lines 16-31). Therefore it would be obvious to use an automated stainer to stain the tissue samples in a high-throughput manner in the method disclosed by Leighton, in order to examine large numbers of tissue specimens.

18. With respect to claim 2, Leighton teaches the use of tissue microarrays (column 1, lines 29-43).

19. With respect to claims 3 and 4, Leighton teaches the staining of tissue samples to reveal structures of interest (column 7, lines 52-57). Leighton does not teach the use of an automated stainer. However, Kalra et al teaches that modern laboratories find it desirable to automate the staining process examine large numbers of tissue specimens (column 1, lines 16-31). Therefore it would be obvious to use an automated stainer to stain the tissue samples in the method disclosed by Leighton, in order to examine large numbers of tissue specimens.

20. With respect to claims 5-6, Leighton teaches a clinical utility of target molecules comprising use in a particular therapy, such as a drug (column 2, lines 15-21).

21. With respect to claim 7, Leighton teaches a clinical utility comprising validation that target is relevant in a particular tissue (column 1, lines 44-57).

22. With respect to claim 8, Leighton teaches that "a plurality of target molecules are provided from a plurality of sources". Specifically Leighton discloses that the tissue microarrays can "analyze hundreds of molecular markers in the same set of specimens" (column 1, lines 30-43, column1, line 58 – column 2, line 1)

23. With respect to claim 11, Leighton teaches an array that can be used for parallel *in situ* detection of DNA, RNA, and protein targets in each specimen on the array (column 2, lines 1-8).

24. With respect to claim 12, Leighton teaches an array comprising a different tissue samples mounted on a solid support. Specifically Leighton discloses a multi-specimen tissue block where "biological tissue arrays are constructed simply as arrays (rows and columns) of cores of biological tissue, each core having been punched from an individual donor tissue sample and embedded at a specific grid coordinate location in a sectionable block typically made of the same embedding material used for the donor tissue (column 2, lines 10-33).

25. With respect to claim 13, the method is high-throughput (column 1, lines 30-43).

26. With respect to claim 17-19, Leighton teaches a tissue microarray that has a solid surface with tissue samples mounted to the solid surface (column 1, lines 57-68). Leighton does not teach the use of a bar code labeled slide for identifying how the tissues are to be treated by a machine. Kalra et al, however, does teach the use of slides with bar code labels for optional features that can be included on the apparatus include devices intended to ensure level operation,

to protect against electric shock, to verify that an appropriate tip has been selected and properly placed on the tip head, or to optically scan slides in a microscope slide tray or other container for microscope slides so that a user is not required to enter information into the computer (column 20, lines 56-63). Therefore, it would be obvious to use slides with bar-code labels in the method of Leighton so that a user is not required to enter information into the computer.

27. With respect to claim 20, Leighton does not teach a treatment comprising automated staining of tissues. However, Kalra et al teaches that laboratories find it desirable to automate the staining process examine large numbers of tissue specimens (column 1, lines 16-31). Therefore it would be obvious to use an automated stainer to stain the tissue samples in a high-throughput manner in the method disclosed by Leighton, in order to examine large numbers of tissue specimens.

28. Claims 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leighton [US 6,103,518], in view of Kalra [US 6,495,105] as applied to claims 1-13, 17-20 above, and further in view of Bogen et al [US 6,183,693]. Leighton teaches a method for evaluating the clinical utility of target molecules comprising the steps of providing a large quantity of different tissue samples, providing a target molecule, providing a stain that specifically binds to said target molecule *in situ*, applying in a high-throughput manner said stain to said tissue samples and determining the extent to which said stain has bound to said target molecule in said tissue samples. Specifically, Leighton discloses the use of a tissue chip, "a thin section of a tissue microarray that permits massive parallel processing of biological samples, making it possible for researchers to simultaneously compare a variety of molecular markers--DNA, RNA, and protein--in cancer tissues from hundreds or thousands of patients," allowing for the simultaneous testing

of thousands of patient tissue specimens which pathology laboratories have traditionally analyzed one specimen at a time (column 1, lines 30-43). Furthermore, Leighton teaches the staining of tissue samples to reveal structures of interest (column 7, lines 52-57). Leighton does not teach an instrument comprising a first heater and a second heater. Bogen, however teaches that since various staining procedures require heat at different times to enhance the rate of chemical reaction, a means has been developed to heat slides to different temperatures, independently of the temperatures of other slides (column 1, line 60-column 2, line 5). Therefore it would be obvious to use an instrument with multiple heaters in the method of Leighton, as taught by Bogen, in order to enhance the rate of chemical reaction during staining.

29. With respect to claims 15 and 16, Leighton does not teach the limitation of an instrument with heaters mounted to a carousel with means for monitoring and controlling the temperature of the heaters. Bogen et al, however, teaches a carousel adapted to support a plurality of microscope slides bearing biological samples. A plurality of flat heating stations are provided on the platform, each heating station supporting at least one microscope slide and, in a preferred embodiment, each heating surface supporting a single microscope slide. The heating stations are individually controlled to control temperatures to which the slides are heated (column 2, lines 33-44), since various procedures require heat at different times to enhance the rate of chemical reaction (column 1, line 60-column 2, line 5). Therefore, it would be obvious to include multiple heaters mounted on a carousel with means for monitoring and controlling the temperature of the heaters, as taught by Bogen, in order to enhance the rate of the chemical reaction during staining.

Conclusion

30. No claims are allowed.

31. The following references are also cited as art of interest: Chan etl al [US 5,120,662], Christensen et al [US 6,544,798 B1], Bacus et al [US 5,428,690], Bacus et al [US 6,466,690], Molnar et al [US 6,246,785 B1], Wiegel [US 6,107,034], Nodine et al [US 3,856,930], Griffith et al [US 6,197,575 B1]

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is 703-305-4508. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V Le can be reached on 703-305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

NY

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
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